VI: MICROBICIDES

AREA OF EMPHASIS:

Microbicides

SCIENTIFIC ISSUES

There is an urgent need to expand the range of interventions for preventing HIV transmission. It is not known when a safe and effective vaccine will be developed, and even when such a vaccine will become available, it is acknowledged that a vaccine will be only one of a variety of approaches to preventing HIV infection. At present, the most promising vaccine candidates do not provide protection from infection, but alter its course by lowering the levels of viremia. Thus, primary prevention approaches are still needed as complementary interventions. Microbicides, defined as antimicrobial products that can be applied topically for the prevention of sexually transmitted infections (STIs), including HIV, may offer one of the most promising primary preventive interventions that could be safe, effective, readily available, and widely acceptable. Microbicides used alone or in combination with physical barriers could be used both by HIV-infected individuals to prevent transmission to their partners and by uninfected individuals to protect themselves from acquiring HIV. A consensus has emerged across the STI and AIDS research communities that development of microbicides presents an important opportunity and challenge for scientific investment.

The impact of AIDS on developing nations of Africa, Asia, Latin America, the Caribbean, and the former Soviet Union countries is staggering, with even greater numbers of projected new infections to come. In these countries, heterosexual transmission is the predominant mode of HIV spread. Recent data indicate that worldwide there are now almost equal

numbers of men and women infected with HIV. In sub-Saharan Africa, the area hardest hit by the pandemic, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimated that 19.2 million women were living with HIV/AIDS at the end of 2002, a number nearly equal to that of HIV-infected men. Of the more than 14,000 estimated new infections every day, half occur in young persons between the ages of 15 and 24, and female adolescents are disproportionately affected compared to boys. Attitudes, beliefs, and taboos surrounding sexual activity, the status of women and children, and the lack of understanding in regard to factors that enhance susceptibility also complicate development of strategies to prevent transmission of HIV.

Although the incidence of new AIDS cases in the United States has declined with the expanded use of new antiretroviral therapies (ART), the initial steep decline in death rates observed in the late 1990s has leveled off. According to the Centers for Disease Control and Prevention (CDC), the rate of new HIV infections has been constant, indicating that the overall epidemic is continuing to expand. In fact, HIV infection rates are continuing to climb in a number of subpopulation groups, including women, racial and ethnic minorities, young homosexual men, and people more than 50 years of age. In the United States, more than 30 percent of newly reported HIV cases diagnosed are occurring in women, according to the most recent data collected by the CDC. As in the rest of the world, the majority of these reported HIV infections among U.S. women result from heterosexual transmission, and the data suggest that younger women are disproportionately at risk for acquiring HIV. As these women are likely to become pregnant and have children, mother-to-child transmission may increase, even in the face of effective and affordable preventive measures.

Prevention programs that promote abstinence, faithfulness, and condom use require a certain level of communication and negotiation between partners. For many women in both developed and developing countries, negotiating safer sex may not be possible. Women, especially in developing countries, are economically, culturally, and socially marginalized. As a result, male/female power relations are not balanced, and women become infected because they cannot insist on condom use or cannot protect themselves from nonconsensual, coercive sex. Many monogamous women are infected during intercourse with their husbands, who may not be monogamous, suggesting that microbicides are needed for use by women in their primary partnerships.

In response to this urgent need, the NIH AIDS prevention research agenda has made a high priority the development of chemical and physical barriers

that can be applied topically to the epithelial surfaces exposed to HIV during sexual intercourse. The NIH has a comprehensive research program that includes the screening, discovery, development, preclinical *in vitro* and *in vivo* testing, and clinical evaluation of compounds that have the potential to act as antimicrobial agents. Social and behavioral studies also are conducted to evaluate the possible acceptability and use of such agents. The NIH closely collaborates with academia and industry to identify and explore new and existing compounds as potential topical microbicidal agents.

NIH-sponsored contracts support animal model testing and toxicity studies of potential lead compounds before these agents are considered for clinical trials. The NIH also supports Phase I, II, and III clinical trials of potential microbicides in both domestic and international settings. Currently several categories of compounds are undergoing thorough testing: cell/pathogen surface disruptive agents that kill or inactivate viruses and pathogens; inhibitors of viral binding and fusion/entry into susceptible cells; enhancers of normal vaginal defense mechanisms; and inhibitors of HIV replication (antiretroviral drugs such as nucleoside and nonnucleoside reverse transcriptase inhibitors). Some of these products are nonspecific and have both spermicidal and antimicrobial activity against HIV and other pathogens, and some specifically interfere with HIV attachment and entry or the ability of the virus to replicate once it has entered a susceptible cell.

The NIH AIDS prevention research agenda has also made the evaluation of acceptability and use of microbicides among diverse populations a high priority within its portfolio of behavioral and social science research. These data are essential to ensure that these agents will be used by those at risk in order to halt the further sexual transmission of HIV and other STIs.

PRIORITY FOR FUTURE RESEARCH:

- **Foster the development of microbicides consisting of exogenous and endogenous agents and based on specific biological and physiological pathways involving HIV transmission across the epithelia.**

Basic biological and physiological research is of fundamental importance for the field of microbicides research. Translation of basic insights into HIV biology and pathogenesis, knowledge of the different steps required for HIV transmission and local propagation at mucosal/epithelial surfaces, and a better understanding of immune responses in the reproductive tract are essential for identifying new targets for microbicides discovery and development. Early work has focused on nonspecific inhibitors of HIV. However, specific approaches hold the greatest promise

for microbicides that would be effective at very low concentrations without interfering with normal cellular processes. Therefore, there is a clear need to increase our understanding of the basic mechanisms and factors influencing HIV transmission at mucosal/epithelial surfaces in order to identify multiple safe and effective strategies for blocking the early steps in the infectious process. Important areas of research include the identification of new viral and host targets for microbicide discovery, the determination of the first cell or tissue type that becomes infected and locally propagates HIV infection as well as the nature of the actual infectious unit, the elucidation of the impact of microbicides on regional/local immune responses, the understanding of physiologic changes that occur during intercourse, the elucidation of the mechanism by which inflammation and/or concomitant infections influence HIV transmission, and the investigation of the effects of endogenous and exogenous hormonal states on the susceptibility to infection. Emphasis should also be placed on studies of the normal vaginal ecology, since the ideal microbicide should not disrupt each ecosystem's integrity and balance. An understanding of the components of these ecosystems and their function, as well as the effect of microbicides use on these environments, is essential to the development of safe and effective topical microbicides.

PRIORITY FOR FUTURE RESEARCH:

- **Identify and standardize relevant, practical, and accessible methodologies to assess preclinical/clinical safety and activity of microbicides.**

An effective translation of basic insights into HIV biology and pathogenesis is also important for developing and validating relevant *in vitro* and *in vivo* models to assess safety and efficacy of active agents and formulated microbicide products. This is an area of utmost importance since the preclinical evaluation of microbicidal products should support the rationale for clinical testing in humans by providing a clear description of activity against HIV and other STIs in the absence of local and systemic toxicity in animal models. Because topical microbicides will be used predominately by HIV-uninfected individuals, the standards for safety of regular use are higher than for therapeutics where the risk/benefit ratio generally favors treatment. However, many of the methods for evaluating safety are borrowed from the drug development and the contraceptive fields and might not be either relevant or appropriate for testing microbicides. *In vitro* safety studies using tissue culture cell lines or human tissue explants are of uncertain clinical relevance, and we do not have a complete understanding of the most important indicators of safety in human

studies. Efforts to standardize the most relevant methodologies so that the results from different studies can be compared would greatly accelerate progress in this field.

The lack of a well-established correlation between *in vitro*, animal models, and clinical testing; the insufficient knowledge about the biology of sexual transmission of HIV and other STIs; the lack of optimal formulations or an adequate understanding of the biophysical and chemical effects of formulation on virus transmission; and the insufficient knowledge on cervicovaginal and intercourse physiology are posing formidable challenges to rapid progress in this field and should represent the target of intense investigations by NIH-sponsored researchers.

PRIORITY FOR FUTURE RESEARCH:

- **Foster the development of combination approaches, such as chemical and physical barriers, and of microbicides containing multiple active compounds with different chemical classes, specificities, and mechanisms of action in acceptable formulations to prevent transmission and acquisition of HIV and other STIs.**

Microbicides can be available alone or in combination with different agents within the same product or in combination with physical barriers. Protection of the cervix, which may have increased susceptibility to HIV infection, may require the additional level of protection provided by a physical barrier. In addition, different active agents in the same products might act synergistically or sequentially against a single pathogen or expand the range of activity against other pathogens. The ideal microbicide needs to be effective against a range of sexually transmitted viruses and pathogens. This is of particular importance for HIV prevention efforts, since other STIs have been shown to promote the transmission of this virus. A broader range of microbicidal activity can be achieved by combining agents against other viruses or pathogens in a single product. For example, a combination of nonspecific inhibitors of viral attachment such as sulfated or sulfonated polymers with specific inhibitors of HIV entry may offer a specific chemical barrier against HIV, while also protecting against other types of infections such as herpes simplex virus (HSV).

PRIORITY FOR FUTURE RESEARCH:

- **Promote innovative methods to develop and assess acceptable formulations and modes of delivery for microbicides, bridging knowledge and applications from multiple scientific disciplines.**

One of the most challenging steps in the development of safe, effective microbicides is combining the active microbicidal agents into vehicles, such as gels, creams, foaming tablets, suppositories, rings, or rapidly dissolving films, that will enable delivery to the vagina and inactivation of infectious pathogens in the ejaculate and cervical/vaginal compartments. Formulation expertise is essential at the earliest stages of drug development to ensure optimal performance characteristics and stability of the product. In addition, the delivery mechanism and product attributes will affect end user acceptance and, therefore, need to be assessed in a variety of user populations. Different users will have diverse views regarding the optimal characteristics of a topical formulation. Recent development of devices such as vaginal rings or traditional patches for sustained delivery of antimicrobial agents or hormones have greatly expanded microbicide delivery options. Because formulations will have an impact on both microbicide activity and acceptability, integration of behavioral research on use and acceptability should be considered as active agents are formulated into microbicidal products.

Vaginal products have been successfully formulated by the private sector and provide a framework in which to consider some of the characteristics of the formulated product. The ideal formulation should provide a uniform and durable protection at mucosal/epithelial sites without compromising the integrity of the mucosa, perturbing the local ecology, or resulting in high levels of systemic absorption. Formulations can have a major impact on microbicidal products' performance by either enhancing or decreasing the activity and/or toxicity of the active agents. However, the interaction of formulation excipients on the active agents has been largely unexplored. The field of microbicides will clearly benefit by the development of formulations that, when used alone without active agents, would have no measurable impact on product performance and therefore could be used as inert placebos in clinical trials.

The science of vaginal formulations is very complex, drawing knowledge and expertise from multiple disciplines and sectors, and is a critical component of the effort to develop safe and effective microbicides.

PRIORITY FOR FUTURE RESEARCH:

- **Expand capacity (infrastructure and human resources) and strengthen coordination to conduct Phase I/II/III microbicides clinical trials.**

After preclinical evaluation, the most promising candidate microbicides should be clinically evaluated in humans for safety and effectiveness. Safety studies (Phase I/II) are necessary to evaluate the potential for systemic absorption and toxicity as well as local toxic effects such as erithema, ulceration, or symptoms like itching and burning. Irritation and ulceration of the vaginal, cervical, and penile epithelia may compromise the integrity of epithelia at those sites with a concomitant increase in the risk of HIV and STI transmission. Moreover, all adverse effects have a negative impact on the acceptability of microbicides and influence the future use of these products.

Efficacy/effectiveness studies (Phase IIb/III) are essential to assess whether these products prevent infection with HIV or other STIs, depending upon the product indication. Microbicide trials present a complex variety of challenges in that they require huge and complex efficacy and effectiveness studies that must be conducted in areas with high HIV incidence rates; such rates occur predominantly in developing countries with minimal research infrastructure resources. Microbicide trials, like vaccine trials, are community-based and require the support of the community in which they are going to be conducted. The ethical obligation to provide behavioral counseling and availability of condoms to the study subjects adds to the complexity and size of the trials. The first Phase III clinical studies of candidate microbicides have raised problematic issues that have prompted a reevaluation of timing and methodologies for microbicides trials. Several ways of streamlining this phase of development are now under consideration, including running parallel studies on a given product and testing multiple products in a single trial. Other important areas of research include the establishment of clinical trial sites and the necessary clinical, laboratory, and data management infrastructure to conduct those trials, especially in developing countries; the development of criteria for selecting products to be evaluated in clinical trials and for moving them through the different phases of those studies; and research into ethical and behavioral issues impacting HIV prevention clinical trials. Training is an essential component of building the appropriate infrastructure to conduct clinical studies in developing countries as well as the involvement of communities in the planning and undertaking of international microbicide research. Emphasis should be placed on the development of local institutional review boards (IRBs) and community advisory boards.

Work with national and international regulatory bodies to address regulatory issues should proceed in parallel, in order to promote the rapid development of microbicides. Collaboration with industry, as well as Government and nongovernment organizations and foundations, should be encouraged. At the same time, it must also be ensured that clinical studies of microbicides are undertaken with high ethical standards.

PRIORITY FOR FUTURE RESEARCH:

- **Conduct social and behavioral research in concert with microbicides clinical trials, including research on product use, user acceptability, sexual behaviors, and the identification and development of reliable and valid behavioral tools and measurement techniques for use in trials.**

The effectiveness of any microbicide will depend upon its adoption and continued use by individuals and couples, as well as upon its acceptance and promotion by health care providers. Social and behavioral research on how the choice, acceptability, and use of microbicides affect and are affected by a variety of social, psychological, and cultural factors is an essential element of preclinical and clinical studies. To date, little is known about how people can and might incorporate the use of microbicides into their sexual practices, as these vary across different cultures, ages, and stages of the life course.

To date, most microbicide-related behavioral research, specifically "acceptability" research, has focused on identifying optimal product characteristics for a broad range of potential users. But it is equally important to develop methods for assessing the probability that a microbicidal product actually will be adopted and used consistently and correctly (not just be deemed theoretically "acceptable) in a defined population. Emphasis should be placed on developing valid and reliable behavioral measures that will effectively predict and assess the actual use of microbicides in the context of specific sexual behaviors and different types of sexual partners, and on understanding what attributes will enhance the likelihood of users' selecting the product from the other preventive options available. This knowledge should inform recruitment into clinical trials, design of trial products and protocols, and postmarketing evaluations.

Thus, research is needed on social and behavioral factors related to product use both in the context of clinical trials and among different populations once these products are shown to be effective. Such research should involve both microbicide users and their sexual partners, and should be conducted in parallel with the development of different formulations of microbicidal products.

PRIORITY FOR FUTURE RESEARCH:

- **Promote innovative mechanisms of funding to attract additional investigators to undertake multidisciplinary research on microbicides discovery and development.**

Although data from simian immunodeficiency virus (SIV) challenge studies of microbicides in nonhuman primates are encouraging, there are no clinical data as yet establishing that any product applied topically in humans can prevent HIV infection. Since microbicides have been under development for more than a decade, there is a general perception that there has been insufficient progress in this area. Many factors may have contributed and continue to contribute to this lack of progress, including important scientific challenges presented by aspects of microbicides research and development.

One of the major challenges to progress is the requirement for a complex multidisciplinary and multisectoral approach by teams of scientists with expertise ranging from the biomedical to the behavioral and social sciences to experts in clinical trials and drug discovery and development. Since the field of microbicides is a relatively new specialization in prevention research, there are few acknowledged experts and a limited number of researchers working in the area. A major problem is the paucity of clinical investigators with expertise in all aspects of clinical trial research of new drugs or formulated active agents under evaluation. This is particularly true at international sites where the HIV epidemic is increasing most rapidly. Therefore, there is an urgent need for more researchers to become involved in the field of microbicides. Research innovation and progress require a critical mass of both experienced and new investigators, many of whom have not traditionally engaged in research collaborations. More creative and innovative mechanisms should be created and implemented to attract new scientists to this research area, since conventional funding mechanisms might not be the most appropriate.

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE - A:

Elucidate basic mechanisms of HIV transmission (virus and host factors) at mucosal/epithelial surfaces that are important for microbicide research and development in diverse populations.

STRATEGIES:

Basic Biological and Physiological Research Related to Microbicides

- Identify and characterize new and understudied viral and host targets important for transmission and early dissemination of HIV in the female and male genital tracts and the rectal (lower gastrointestinal [GI] tract) and oral (upper GI tract) mucosal/epithelial sites that are relevant for microbicide discovery and development.
- Determine the impact of microbicides on innate and adaptive mucosal/epithelial defense mechanisms in the female and male genital tracts.
- Study the impact of microbicides on microbial ecology and their effects on mucosal/epithelial secretions and surfaces.
- Study the physiologic changes that occur during intercourse and discern how they relate to transmission or acquisition of HIV and the safety and activity of microbicides.
- Determine the cells or tissue types that serve as portals of entry and support subsequent spread of HIV/SIV and understand the mechanism of virus dissemination to the lymphoid tissue.
- Determine the role of viral phenotype/genotype/clade/resistance pattern and delineate the relative efficiency of transmission of cell-free and cell-associated virus in secretions at the female and male genital tracts.
- Determine the mechanisms by which genital tract inflammation and/or infections (including STIs) may influence HIV transmission and early propagation.
- Investigate the effect of endogenous hormonal states (puberty, pregnancy, menopause, lactation-induced hypoestrogenic states, and menstrual cycles) and exogenous hormonal states (including oral and injectable contraceptives and hormonal replacement therapy) on the susceptibility of the female and male genital tracts to infection with HIV.

OBJECTIVE - B:

Support the discovery, development, and preclinical evaluation of topical microbicides alone and/or in combination.

STRATEGIES:

Microbicide Development and Preclinical Studies

- Develop, validate, and standardize specific, sensitive, and reproducible methods for quantifying HIV/SIV/chimeric simian/human immunodeficiency virus (SHIV) in mucosal/epithelial tissues and secretions before and after use of microbicides.
- Develop, validate, and standardize specific, sensitive, and reproducible methods for quantifying innate responses in mucosal/epithelial tissues and secretions before and after use of microbicides.
- Develop, validate, and standardize specific, sensitive, and reproducible methods for assaying antimicrobial activities *in vitro*.
- Develop and support animal models that more closely reflect the dynamics of sexual transmission of HIV in humans to evaluate safety and efficacy of potential topical microbicides for prevention of mucosal/epithelial HIV/SIV/SHIV transmission.
- Develop, validate, and standardize *ex vivo* explant models of human or nonhuman primate tissue that might provide a useful approach to: (1) investigate the very early events in HIV or SIV/SHIV transmission and (2) evaluate the activity and toxicity of topical microbicides.
- Determine the extent to which *ex vivo* tissue culture models and animal models are predictive of clinical efficacy and safety.
- Integrate genomics, proteomics, and informatics paradigms, concepts, and methodologies (including microchip-based technology) into microbicide discovery and development research.
- Conduct preclinical studies of potential microbicides to assess immunologic and inflammatory effects, pharmacokinetics, pharmacodynamics, toxicity on the mucosal/epithelial surfaces and secretions (female and male), teratogenicity, transplacental carcinogenicity, and effects on fertility.

- Foster the development of combination approaches, such as chemical and physical barriers, and of microbicides containing multiple active compounds with different chemical classes, specificities, and mechanisms of action.
- Investigate the effect of endogenous hormonal states (puberty, pregnancy, menopause, and menstrual cycles) and exogenous hormonal states (including oral and injectable contraceptives and hormonal replacement therapy) on the safety and activity of microbicides.

OBJECTIVE - C:

Develop and assess acceptable formulations and modes of delivery for microbicides, bridging knowledge and applications from the chemical, pharmaceutical, physical, bioengineering, and social sciences.

STRATEGIES:

Microbicide Formulations and Modes of Delivery

- Develop formulations, dosage, and delivery systems suitable for the genital and GI tracts, so that toxicity and trauma to the tissue are reduced or eliminated.
- Develop formulations that share the same physical and chemical properties of the microbicide formulation but lack antimicrobial activity and toxicity, to serve as placebos.
- Identify and validate methods that improve the understanding of bioadhesion, biodispersion, retention, and distribution of microbicide formulations prior, during, and after intercourse.
- Develop methods to measure tissue and systemic absorption following topical microbicide use.
- Develop and incorporate mechanisms to assess product and delivery mode acceptability in diverse populations of men and women that are culturally sensitive and may be used in all phases of clinical studies or outside the trials setting (e.g., through focus groups, interviews, and rapid assessment methods appropriate for the target audience).
- Understand the biologic mechanisms and physiologic changes that contribute to efficacy and safety of microbicide formulations, including, but not limited to, hormonal status, menstrual cycle, nature of intercourse, pregnancy, frequency of use, and sexual arousal.
- Develop, validate, and standardize methodologies to analyze the physical and chemical properties of individual microbicides, formulated microbicides, and combinations of microbicides, including those derived from natural products.
- Develop methodology and supportive studies to characterize product traits (such as taste, smell, color, and texture) that may affect acceptability and adoption/use of microbicides in diverse populations and for different types of sexual acts.

- Leverage the new sustained-release and solid-phase formulations technology for application in the formulation of microbicides for topical use to prevent the sexual transmission of HIV and other STIs.

OBJECTIVE - D:

Conduct clinical studies of candidate microbicides to assess safety, acceptability, and effectiveness in reducing sexual transmission of HIV in diverse populations in domestic and international settings.

STRATEGIES:

Clinical Trials of Microbicide Products

- Develop and evaluate improved methods to recruit and retain participants for Phase I, II, and III microbicide studies in the United States and abroad.
- Reassess the fundamental epidemiological principles informing clinical trials protocols, including an evaluation of control group selection, statistical power, and appropriate followup time.
- Conduct research on mechanisms to improve clinical trial adherence and compliance with use requirements of products under study.
- Identify, develop, and validate behavioral and biological markers to evaluate safety, effectiveness, and adherence to microbicides, including designing, developing, and evaluating tools to measure product use and acceptability.
- Address ethical issues in the design and conduct of microbicide trials.
- Conduct research on ways to ensure adequate informed consent among participants in microbicide trials.
- Conduct research on the acceptability and effectiveness of microbicides relative to and in combination with other behavioral, preventive, and therapeutic methods.
- Identify and develop improved relevant techniques to evaluate safety of microbicides when applied to genital mucosal/epithelial surfaces during clinical trials.
- Enhance understanding of the significance of clinical findings identified by current methods to evaluate safety, including evaluation of cervicovaginal and penile irritation.
- Study microbicide products in HIV-infected people under treatment to determine their impact on the development of drug resistance, drug-to-drug interactions, and the potential for other adverse events.

- Design, implement, and evaluate Phase IV postmarketing surveillance studies once an effective and safe microbicide has been identified in Phase III trials.

OBJECTIVE - E:

Conduct basic and applied behavioral and social science research to inform and optimize microbicide development, testing, acceptability, and use domestically and internationally.

STRATEGIES:

Social Science Research Related to Microbicides

- Support theory-building and the development of social-behavioral models of risk and protection in the context of microbicide research.
- Conduct research on how microbicide use affects and is affected by psychological and social factors, incorporating a developmental perspective on individual and social influences.
- Develop and evaluate the efficacy and effectiveness of behavioral and social interventions to ensure appropriate microbicide use by various populations in different settings.
- Support services research on the implementation and costs of interventions using microbicides, including studies of dissemination, sustainability, acceptance, and adoption of microbicide interventions by health care providers.
- Improve methods for research, including enhancing survey methods and tools, collecting valid self-report data, collecting behavioral and disease outcomes, measuring change over time, and recruiting and retaining subjects in clinical trials.
- Improve methods for data analysis, including approaches to missing data, nonnormal data, and nonlinear changes.
- Develop and refine mathematical models for linking interventions with changes in HIV and STI incidence, accounting for variations in parameters such as condom use, sexual network membership, and background incidence and prevalence of disease.
- Develop, test, and utilize alternatives to the randomized controlled trial that permit ethical and cost-effective evaluation of microbicide interventions at individual, group, and community levels.

OBJECTIVE - F:

Establish and maintain the appropriate infrastructure (including training) needed to conduct microbicide research domestically and internationally.

STRATEGIES:

Infrastructure

- Establish clinical trial sites and the infrastructure required for Phase I, II, and III studies domestically and internationally.
- Identify gaps in biomedical, behavioral, ethical, clinical, and administrative training in national and international microbicide research sites, and design strategies that respond to these needs.
- Foster microbicide research training activities to foster and develop the acumen of national and international independent investigators (including development of mentor relationships and grant and protocol writing skills).
- Develop strategies to strengthen training and infrastructure for the development of national and international institutional capacity for microbicide research, including the enhancement of laboratory capability, data management/analysis, population-based research, high standards of conduct for clinical research, operational support, and physical infrastructure.
- Address economic and administrative obstacles to microbicide research that encumber research and/or clinical evaluation in national and international arenas.
- Develop training and institutional strengthening strategies to involve national and international communities in the planning and undertaking of international microbicide research. This includes building and maintaining sites for population-based research and ensuring that communities involved in research will be prepared to benefit from the research results.
- Provide NIH representation in the development of partnerships among international and national groups currently engaged in microbicide development, research, implementation, and infrastructure strengthening.

- Provide NIH representation in national and international regulatory bodies to address regulatory issues and structures in order to encourage more rapid streamlined development and use of microbicides.
- Foster and support the development of large-scale production systems for the manufacture of microbicidal active agents.
- Develop strategies to promote the involvement of local governments, communities, and advocacy groups in the identification of priorities for and development of clinical protocols, and to sustain these efforts during the conduct of clinical trials.

FY 2006 OAR Planning Group for Microbicides

FY 2006 MICROBICIDES PLANNING GROUP

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